

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:	UNGER	}	EXAMINER:	ILEANA POPA
SERIAL NO.:	10/652,814		ART UNIT:	1633
FILED:	AUGUST 29, 2003		CONFIRMATION NO.:	2748
TITLE:	NANOPARTICLE ENCAPSULATION SYSTEM AND METHODS			

**DECLARATION OF GRETCHEN UNGER
UNDER 37 CFR §1.132**

Dear Sir:

1. I, Gretchen Unger, Ph.D., am the named inventor of the above-referenced application and the President and Chief Scientific Officer of assignee. I received my B.S. in Chemical Engineering from the University of Kansas at Lawrence, Kansas, and my Ph.D. in Pharmacology from the University of Minnesota at Minneapolis, Minnesota. I have been published in peer-reviewed scientific journals in the areas of targeting bioactive agents to cancer. I have been working in the area of micellar delivery of bioactive agents to cells since at least 1998, and I am of skill in the art in the area of micellar delivery of bioactive agents to cells.

2. I have extensively reviewed and am familiar with U.S. Patent 6,139,819 (Unger, et al., herein, " '819"), including the "Examples" section. I have obtained and carefully reviewed the relevant prior patent applications of Unger et al. as referenced in '819. Additionally, I have obtained and have carefully reviewed the teachings of the relevant journal articles and patents that were cited in '819 as examples of methods to form the particles disclosed in '819.

3. Upon information and belief, it is my opinion that none of the particles disclosed in the "Examples" section in '819 disclose a vesicle of less than about 200 nanometers (i.e., less than 0.2 μ m or microns).

4. Upon information and belief, it is my opinion that the preparatory methods for micelles, listed in Column 60, starting at line 50, of '819, cite conventional methods that do not result in the particles as claimed in the above-referenced patent application.

5. Upon information and belief, it is my opinion that the '819 preparatory methods for particles, listed in the below-referenced table prepared under my direction, do not result in the particles as claimed in the above-referenced patent application having an average diameter of less than about 50 nm (nm). See the below table for specific information regarding the disclosures of the '819 referenced materials regarding size of the resultant particles, as I understand the disclosures.

(Col 22, line 17) Vesicles which are formulated from <u>proteins</u> that may be used to prepare the targeted vesicles are described in:	US 4,572,203	Less than 1.5 microns	Col 7, lines 45-48
	US 4,718,433	2-6 microns	Col 4, lines 64-68
	US 4,774,958	2-20 microns	Col 3, lines 4-8
	US 4,957,656	4-6 microns	Col 5, lines 16-20
(Col 72, line 21) Suitable procedures which may be employed or modified in accordance with the present disclosure to prepare vesicles from <u>polymers</u> include:	US 4,179,546	1-50 microns	Col 1, lines 17-23
	US 3,945,956	6-27 microns	Col 3, lines 63+
	US 4,108,806	0.5 + microns	See U.S. 3,615,972
	Japan 62 286534	"Microcapsules"	Abstract
	Britain 1,044,680	n/a	n/a
	US 3,293,114	2+ microns	Col 2, lines 42-51
	US 3,401,475	8+ microns	Col 4, lines 10-36
	US 3,479,811	2+ microns	Col 3, lines 63-71
	US 3,488,714	8+ microns	See US 3,401,475
	US 3,615,972	0.5 microns +	Col 5, lines 30-34
	US 4,549,872	10-200 microns	Col 1, lines 60-63
	US 4,540,629	5-300 microns	Col 5, lines 19-20
	US 4,421,562	1-500 microns	Col 2, lines 1-2
	US 4,420,442	1-500 microns	Col 2, lines 29-30
	US 4,898,734	50-1100 microns	Col 6, lines 21-26
	US 4,822,534	20-800 microns	Col 3, lines 51-55
	US 3,732,172	Micron + (est)	Col 6, lines 23-26
	US 3,594,326	3-1000+ microns	Col 1, lines 46-48
	US 3,015,128	500 microns	Col 8, lines 42-45
	Deasy, Vol 20	200 nm- 3 microns	p. 229, 232
	Chang, Vol 44	2+ microns	p. 121
	Chang,, Vol 146	5 microns	Fig. 1B

(Col 31, line 44) Methods for preparing vesicles which employ polymers as stabilizing compounds include:	US 5,205,290	1-1000 microns	Col 3, lines 11-17
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6. At Col. 61, lines 12-67, of '819, various methods for preparation of liposomes are described. Upon information and belief, it is my opinion that these referenced methods for preparation of liposomes do not teach methods which will result in the particles of the instant invention, for the reason that the particles of the instant invention are made up of a bioactive component as a core, hydrophobic surfactant molecules, and polymers with specific cell uptake function, the particles having an average diameter of less than about 50 nanometers.

7. Upon information and belief, it is my opinion that the '819 patent, and the patents and journal articles referenced therein, do not contain teachings of any methods for how to make particles of the instant invention, for the reason that the particles of the instant invention are made up of a bioactive component as a core, hydrophobic surfactant molecules, and polymers with specific cell or tissue uptake function, the particles having an average diameter of less than about 50 nanometers.

8. I have personally carried out experiments to try to produce the instantly claimed particles made up of a bioactive component as a core, hydrophobic surfactant molecules, and polymers with specific cell uptake function, the particles having an average diameter of less than about 50 nanometers, using at least one of the materials taught by Unger et al., i.e., polysorbate 80 (TWEEN 80, Col 34 line 3). As discussed in Example 1 in the above-referenced patent application, I found in the course of my experiments use of TWEEN 80 does not result in particles having an average size of under 50 nm.

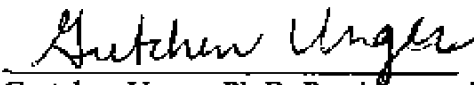
9. In accordance with the discussions in Paragraphs 3-8 herein, and based upon both my knowledge and upon information and belief, and as a person skilled in the relevant art, it is my opinion that at least the portion of the '819 patent that may describe particles as claimed in the above-referenced application, made up of a bioactive component as a core, hydrophobic surfactant molecules, and polymers with specific cell

uptake function, the particles having an average diameter of less than about 50 nanometers, is not enabled, since no methods that result in such particles of such size are described or referenced in '819.

10. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

Date: 12/14/2006



Gretchen Unger, Ph.D, President and Chief
Scientific Officer
GeneSegues, Inc.

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